



(VI)

where R^{10} and R^{11} are independently selected from hydrogen or alkyl, particularly C_{1-4} alkyl.

5 Preferably R^2 is carboxy or a pharmaceutically acceptable salt or ester thereof.

Suitable groups R^3 include hydrogen, fluoro, chloro, bromo, iodo, methyl, cyano, trifluoromethyl, hydroxymethyl, alkoxyalkyl such as C_{1-4} alkoxymethyl, methoxy, benzyloxy, carboxyalkoxy such as carboxymethoxy, methylsulphanyl, methylsulphinyl, methylsulphonyl or carboxy C_{3-6} cycloalkyl, $-(CHR^{23})_r-NR^{23}R^{24}$ (where r is 0-2, each R^{22} is independently

10 hydrogen or alkyl, in particular C_{1-4} alkyl, R^{23} and R^{24} are independently selected from H and C_{1-4} alkyl or R^{23} and R^{24} together with the nitrogen to which they are attached form a 5 or 6 membered ring optionally containing one further heteroatom selected from O, N, S, S(O) or SO_2 . Suitably R^{23} and R^{24} together form a heterocyclic ring such as morpholino or piperazinyl.

Other such groups R^3 include optionally substituted aryl groups, such as optionally
15 substituted phenyl or naphthyl group. Suitable substituents for phenyl groups R^3 include one or more groups selected from chlorine, fluorine, methyl, trifluoromethyl, trifluoromethoxy, amino, formyl, phenyl, methoxy, phenoxy or phenyl.

R^3 may comprise a range of substituents as listed above, in particular, hydrogen or a small substituent group such as C_{1-4} alkyl in particular methyl, or trifluoromethyl, and is
20 preferably hydrogen.

Suitable optional substitutents for the group R^{15} , R^{16} and R^{17} as they appear in the definition of R^4 , include functional groups as hereinbefore defined, as well as aryl or heterocyclyl groups, either of which may themselves be substituted by one or more functional groups or further aryl or heterocyclyl groups.

25 Particular examples of substituents for groups R^{15} , R^{16} and R^{17} include one or more groups selected from halo such as chloro; hydroxy; cyano; amino; mono- or di-alkylamino; C_{1-4} alkoxy; carboxy; sulphonamido; $CONH_2$; alkylamido where the alkyl moiety is optionally substituted for example with a functional groups such as carboxy; morpholino;

pyridyl; pyrimidinyl; phenyl optionally substituted by halo such as chloro, hydroxy, alkoxy such as methoxy, carbamoyl, acyl such as acetyl, or hydroxyalkyl where the alkyl group suitably includes at least two carbon atoms, such as hydroxyethyl. Other examples of substituents for phenyl groups R^{15} is alkanoylamino group such as methoylamino.

- 5 Where R^{15} , R^{16} and/or R^{17} is a heterocyclyl group, or where R^{16} and R^{17} together form an optionally substituted heterocyclic ring, these may be substituted by functional groups such as halo or hydroxy, or by alkyl groups such as methyl or ethyl, or alkenyl or alkynyl groups any of which may be substituted, for example with hydroxy, as well as with further heteroaryl groups such as pyridyl. Particular examples of heterocyclic groups R^{15} , R^{16} and/or R^{17} are optionally substituted thiophenyl, optionally substituted imidazolyl, optionally substituted pyridyl.

- 15 Thus thiophenyl groups R^{15} , R^{16} and/or R^{17} may comprise pyridyl-thiophenyl, whilst an example of a substituted imidazolyl group for R^{15} , R^{16} and/or R^{17} is methylimidazolyl and halopyridyl in particular chloropyridyl is an example of a substituted pyridyl moiety for these groups.

- 20 Particular examples of R^{15} include alkyl in particular methyl optionally substituted by a functional group or, in particular, a heterocyclyl group where the heterocyclyl group may be optionally substituted by a functional group such as halo or hydroxy or by an alkyl group such as methyl. Preferably, R^{15} is a substituted alkyl group. Where the substituent is a functional group, it is preferably a group of formula $NR^{19}R^{20}$ where R^{19} and R^{20} are as defined above. Thus examples of substituted alkyl groups R^{15} include morpholinomethyl or alkyl such as methyl substituted with a substituted alkyl amino group wherein the substituents include carboxy, alkanoyl, phenyl or alkyl sulphonyl.

- 25 Other examples of R^{15} are heterocyclyl groups which are optionally substituted for example by alkyl such as methyl, functional groups such as chloro or heterocyclyl groups such as pyridyl.

Particular examples of R^{16} and R^{17} are alkyl such as methyl.

X is CH_2 or SO_2 and is preferably CH_2 .

- 30 Suitable pharmaceutically acceptable salts of compounds of formula (I) include acid addition salts such as methanesulfonate, fumarate, hydrochloride, hydrobromide, citrate, maleate and salts formed with phosphoric and sulphuric acid. In another aspect suitable salts are base salts such as an alkali metal salt for example sodium, an alkaline earth metal salt for

example calcium or magnesium. an organic amine salt for example triethylamine, morpholine, *N*-methylpiperidine, *N*-ethylpiperidine, procaine, dibenzylamine, *N,N*-dibenzylethylamine or amino acids for example lysine. There may be more than one cation or anion depending on the number of charged functions and the valency of the cations or anions. A preferred

5 pharmaceutically acceptable salt is a sodium salt.

An *in vivo* hydrolysable ester of a compound of the formula (I) containing carboxy or hydroxy group is, for example, a pharmaceutically acceptable ester which is hydrolysed in the human or animal body to produce the parent acid or alcohol.

Suitable pharmaceutically acceptable esters for carboxy include alkyl esters, such as

10 C₁₋₆ alkyl esters for example, ethyl esters, C₁₋₆alkoxymethyl esters for example methoxymethyl, C₁₋₆alkanoyloxymethyl esters for example pivaloyloxymethyl, phthalidyl esters, C₁₋₈cycloalkoxy-carbonyloxyC₁₋₆alkyl esters for example 1-cyclohexylcarbonyloxyethyl; 1,3-dioxolen-2-onylmethyl esters for example 5-methyl-1,3-dioxolen-2-onylmethyl; and C₁₋₆alkoxycarbonyloxyethyl esters for example
15 1-methoxycarbonyloxyethyl and may be formed at any carboxy group in the compounds of this invention.

Suitable pharmaceutically acceptable esters of compounds of formula (I) are *in vivo* hydrolysable ester of a compound of the formula (I) containing a hydroxy group includes inorganic esters such as phosphate esters and α -acyloxyalkyl ethers and related compounds
20 which as a result of the *in vivo* hydrolysis of the ester breakdown to give the parent hydroxy group. Examples of α -acyloxyalkyl ethers include acetoxymethoxy and 2,2-dimethylpropionyloxymethoxy. A selection of *in vivo* hydrolysable ester forming groups for hydroxy include alkanoyl, benzoyl, phenylacetyl and substituted benzoyl and phenylacetyl, alkoxycarbonyl (to give alkyl carbonate esters), dialkylcarbamoyl and
25 *N*-(dialkylaminoethyl)-*N*-alkylcarbamoyl (to give carbamates), dialkylaminoacetyl and carboxyacetyl.

Esters which are not *in vivo* hydrolysable are useful as intermediates in the production of the compounds of formula (I) and therefore these form a further aspect of the invention.

Thus examples of compounds of formula (I) include the following: